TEST PLAN FOR THIODIPROPIONITRILE (CAS NO. 111-97-7)

OVERVIEW

The Thioesters Association agreed to sponsor thiodipropionitrile (CAS No. 111-97-7) in the U.S. EPA High Production Volume Chemical Program. The sponsors hereby submit a revised, final test plan for this substance. All testing proposed in the previous test plan has been completed. Existing plus modeled data now fulfill all Screening Information Set (SIDS) endpoints.

Table 1. Test Plan Matrix for Thiodipropionitrile (CAS No. 111-97-7)

CAS No. 111-97-7	Information	Estimation	Acceptable	New Testing Required
ENDPOINT	Y/N	Y/N	Y/N	Y/N
PHYS/CHEM PROPERTIES				
Melting Point	Y	N	Y	N
Boiling Point	Y	N	Y	N
Vapor Pressure	Y	N	Y	N
Partition Coefficient	Y	Y	Y	N
Water Solubility	Y	N	Y	N
ENVIRONMENTAL FATE				
Photodegradation	Y	Y	Y	N
Stability in Water	Y	N	Y	N
Biodegradation	Y	N	Y	N
Transport between Environmental Compartments (Fugacity)	Y	Y	Y	N
ECOTOXICITY				
Acute Toxicity to Fish	Y	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y	Y	N
Toxicity to Aquatic Plants	Y	Y	Y	N
TOXICOLOGICAL DATA				
Acute Toxicity	Y	N	Y	N
Repeated Dose Toxicity	Y	N	N	NR
Genetic Toxicity-Mutation	Y	N	Y	N
Genetic Toxicity-Chromosomal Aberrations	Y	N	Y	N
Toxicity to Reproduction	N	N	N	NR
Developmental Toxicity	N	N	N	NR
OTHER TOXICITY DATA				
Skin Irritation	Y	N	Y	N
Eye Irritation	Y	N	Y	N
Sensitization	Y	N	Y	N

Y = yes; N = no; NR = toxicity testing is not required because the material is a closed system intermediate (see Appendix I).

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1. Introduction

The Thioesters Association agreed to supply screening information under the U.S. EPA High Production Volume Chemical Program for thiodipropionitrile (TDPN). The test plan was first submitted to the Environmental Protection Agency and posted on the EPA HPV Chemical Challenge Program website in January 2004. A response to EPA comments was posted in September 2004. In agreement with the EPA, the sponsors have conducted studies on biodegradation, mutation and chromosomal aberration to address initial deficiencies of data for these endpoints. These endpoints have now been addressed satisfactorily, and the study robust summaries have been added to the dossier for this chemical. The test plan has been appropriately revised to reflect the newly generated test data, and the dossier and test plan are now considered final for the purposes of the U.S. HPV Chemical Challenge Program.

2. Designation of Test Substance

The test substance presented in this test plan is 3,3'-thiodipropionitrile (CAS No. 111-97-7). Its chemical structure is as follows:

$$NCCH_2CH_2SCH_2CH_2CN$$

This substance has the following synonyms:

Di(2-cyanoethyl)sulfide
Propionitrile, 3,3'-thiodi
Sulfide, bis(2-cyanoethyl)
Thiodipropionitrile

3. Criteria for Determining Adequacy of Data

All available studies were reviewed and assessed for adequacy according to the standards of Klimisch et al. (1997). Studies receiving a Klimisch rating of 1 or 2 were considered to be adequate.

4. Discussion of Available Test Information

The thiodipropionitrile test plan matrix (as shown in Table 1) was constructed after a careful evaluation of all existing data (see below). This matrix is arranged by study type (columns) and screening data endpoints (rows), and indicates if data are provided for each end point in the sets of robust summaries.

4.1 Chemical and Physical Properties

The results of chemical/physical property testing are shown in Table 2.

Table 2. Chemical/physical properties of thiodipropionitrile

Endpoint	Thiodipropionitrile (CAS No. 111-97-7)
Molecular weight grams/mol	140.20
Melting point	25 – 29 ºC[a]
Boiling point	163-4 ºC at 1 hPa[a]
Relative density	1.11[a]
Vapor pressure	7.3 x 10E-5 hPa[a] at 25° C
Partition coefficient (Log Pow or Kow)	-0.05 [b]
Water solubility (mg/l at 30 ° C)	25,000 [a]

[a]measured; [b] estimated by EPIWIN

4.1.1 Melting Point

A measured melting point of 25 – 29 ºC was obtained in a recent study conducted according to OECD Test Guideline 102 (Cuthbert and Mullee, 2003). A melting point of 25ºC is reported by the Cytec Industries Inc. material safety data sheet. The results are consistent with the physical state of the product at room temperature. The product is in the form of a solid or liquid, or is partially solid at ambient temperatures (20-30ºC), depending on whether the purity is 96.5% or closer to 99%.

4.1.2 Boiling Point

A measured boiling point of 163-4 ºC at 1 hPa has been reported in the Dow Chemical Company material safety data sheet for thiodipropionitrile.

4.1.3 Vapor Pressure

A vapor pressure of 7.3 x 10^{-5} hPa at 25° C has been measured using OECD Test Guideline 104 (Tremain, 2003). The EPIWIN MPBPWIN calculated value is 0.03 hPa at 25° C. Measured inputs to the model were a melting point of 27 ° C, boiling point of 250 ° C at 1013 hPa, vapor pressure of 5.5 E-5 mm Hg, and a water solubility of 25,000 mg/l.

4.1.4 Octanol/Water Partition Coefficient

The EPIWIN KOWWIN program provides a calculated partition coefficient of log Kow = –0.05. Measured inputs to the model were a melting point of 27° C, boiling point of 250 ° C at 1013 hPa, vapor pressure of 5.5 E-5 mm Hg, and a water solubility of 25,000 mg/l.

4.1.5 Water Solubility

A measured water solubility value of 25,000 mg/l at 30ºC has been reported in the Cytec Industries Inc. material safety data sheet for thiodipropionitrile. The EPIWIN WSKOW program calculates a water solubility of 117,900 mg/l at 25°C.

4.1.6 Summary/Test Plan for Physical Properties

Measured values are available for melting point, boiling point, vapor pressure and water solubility. These values are considered to be sufficient to characterize these endpoints. A calculated value is available for the partition coefficient, using EPIWIN KOWWIN. This value is deemed to be adequate to characterize this endpoint.

4.2 Environmental Fate/Pathways

Results of environmental fate modeling and studies are summarized in Table 3.

Table 3. Environmental fate parameters for thiodipropionitrile

Endpoint	Value
Indirect Photolysis (OH sensitizer) (Hydroxyl Radical Rate Constant)[b] (Atmospheric $T_{1/2}$) [b]	 3.885 E-12 cm3/(molecule*sec) 33 hours
Stability in Water[a]	$T_{1/2}$ > 1 year at 25 º C
Henry's Law Constant[b]	2.38 E-10 atm-m^3/mol
Koc[b]	177.1
Environmental transport (Fugacity Level III mass percentages)[b]	Air = 0.007 Water = 49.3 Soil = 50.6 Sediment = 0.0917
Biodegradation	No biodegradation

[a]measured; [b] Estimated using EPIWIN; [c]OECD 301F

4.2.1 Photodegradation

Photodegradation with hydroxyl radical sensitizer was estimated using EPIWIN/AOP (v1.90). An overall OH rate constant of 3.885 E-12 cm^3/(molecule*sec) was calculated based on the summation of individual rate constants for each bond fragment in the molecule using the program algorithm. A half-life of 33 hours was calculated assuming a constant concentration of OH radical and pseudo first order kinetics.

4.2.2 Stability in Water

According to a recent study conducted according to OECD Test Guideline 111 (Cuthbert and Mullee, 2003), less than 10% of the material hydrolyzes over 5 days in solutions maintained at pH values of 4, 7 and 9 and a temperature of 50 +/- 5 degrees C, and at a physiologically relevant pH and temperature (1.4 and 37 degrees C, respectively). The half-life calculated from the data at pH 4, 7 and 9 was > 1 year at 25 degrees C. However, according to manufacturing information (see Appendix I), hydrolysis of thiodipropionitrile to the corresponding acid salt has been observed at temperatures higher than those used for manufacture (28 - 30ºC).

4.2.3 Fugacity

Level III fugacity modeling has been conducted on the test material using the EPIWIN model. Measured inputs to the program are the melting point, boiling point, and water solubility listed in Table 2. Emission rates inputted into the program were air: 0 kg/hr, water: 1000 kg/hr, soil: 1000 kg/hr and sediment: 0 kg/hour. The following half-lives were calculated: T ½ air = 66 hr, water = 900 hr, soil = 900 hr, and sediment = 3600 hr. The Biowin ultimate value range was weeks to months. A Henry's Law Constant of 2.38 E -10 atm-m^3/mol and a soil sediment partition constant (Koc) of 177.1 were estimated using the EPIWIN/HENRY and PCKOC Programs, respectively. The percent mass balances predicted for thiodipropionitrile in air, water, soil and sediment are shown in Table 3. The results indicate that the material will partition to water and soil.

4.2.4 Biodegradation

An OECD Test Guideline 301F (Manometric Respirometry Test) has been conducted with 54 mg/l of TDPN and dilute, activated sludge containing 30 mg/l of dry solids (Marty and West, 2004). The OECD 301F is a ready biodegradation test. No biodegradation was observed in the test at levels which appeared to be inhibitory to the microbial inoculum. The study was given a reliability rating of 1 (valid without restriction), since it was a guideline study with no deviations. While the test results suggest the material is not readily biodegradable, it does not mean the material is not readily or inherently biodegradable at lower concentrations.

4.2.5 Summary/Test Plan for Environmental Fate Parameters

Estimated values are available for the hydroxyl radical induced photolysis rate constant and atmospheric half-life, Henry's Law Constant, soil sediment partition coefficient, and Fugacity Level III environmental transport parameters. No further testing is planned for these endpoints. Results of recent tests indicate that the material is fairly stable in water and is not readily biodegradable.

4.3 Ecotoxicity

No measured data are available for aquatic toxicity of TDPN. Eastman and Solutia have filed an HPV test plan for the alkyl nitriles, which includes the related materials propionitrile, butyronitrile and isobutyronitrile (http://www.epa.gov/chemrtk/alkyntrl/c14860tp.pdf). Experimental and ECOSAR-modeled data for these materials, along with ECOSAR-modeled data for TDPN (as shown in Table 4 below), will be used to fill aquatic toxicity endpoints for TDPN. Since propionitrile is most similar to TDPN, aquatic toxicity data for this material will be used preferentially (if available).

4.3.1 Acute Toxicity to Fish

The toxicity of the related material propionitrile has been tested in fathead minnows in a flow through study (Geiger et al., 1990) and in bluegill sunfish and rainbow trout in static studies (ABC Laboratories Inc., 1981a,b). The 96-hour LC50 values (with confidence limits) for the respective species were 1520 (1450-1580) mg/l (measured concentration), 41 (28-66) mg/l (nominal concentration), and 340 (180-560) mg/l (nominal concentration).

Table 4. Aquatic toxicity data for thiodipropionitrile and related alkyl nitriles

Species	TDPN Predicted by ECOSAR	Nitrile Predicted by ECOSAR	Propionitrile Measured
Fish LC50	8785 mg/l	1452 mg/l (Propionitrile)	1520 mg/l (fh minnow)[a] 340 mg/l (trout) [b] 41 mg/l (bluegill) [b]
Daphnia EC50	8171 mg/l	1388 mg/l (Propionitrile)	250 mg/l [c]
Algae EC50	4540 mg/l	789 mg/l (Propionitrile) 365 mg/l (Butyronitrile) 430 mg/l (Isobutyronitrile)	N.D. > 133.4 > 87.8

LC50 = lethal concentration in 50% of organisms, EC50 = concentration required for 50% inhibition of growth, fh = fathead, N.D. = not determined
[a] Flow through; [b] Static; [c] LC50

The 96-hr LC50 values for TDPN and propionitrile in fish estimated by the EPA's ECOSAR neutral organics model are 8785 and 1452 mg/l, respectively.

For propionitrile, with the exception of the bluegill, all predicted values are within 10 times of measured value. In the bluegill study, dissolved oxygen levels decreased from 0 to 96 hours, with the dissolved oxygen levels ranging from 2.0-4.3 at the end of the study. According to the propionitrile dossier, the lowest dissolved oxygen concentration was observed in water with the highest concentration of propionitrile. The low dissolved oxygen values are obvious confounders to the bluegill data. The more reliable fish toxicity studies for propionitrile lend support to the conclusion that measured LC50 values for TDPN in fish should be no less than 10 times lower than the predicted value of 8785 mg/l.

4.3.2 Acute Toxicity to Aquatic Invertebrates

A static, 48-hour toxicity test to *Daphnia magna* has been performed with the related material propionitrile (ABC Laboratories, Inc., 1981c). The 48-hour LC50 value (with confidence limits) was 250 (210-290) mg/l (nominal concentration). A reliability rating of 2 (valid with restrictions) was assigned since concentrations of material were not analytically confirmed.

The EPA's ECOSAR neutral organics model predicts a 48-hour EC50 values of 8171 and 1388 mg/l for TDPN and propionitrile in Daphnia (respectively). For propionitrile, the predicted EC50 value is within 10 times of the LC50 measured value. This comparison suggests that the measured EC/LC50 value for TDPN in Daphnia should be no less than 10 times lower than the predicted value of 8171 mg/l.

4.3.3 Acute Toxicity to Aquatic Plants

The 96 hr EC50 values calculated for TDPN and propionitrile in green algae by the ECOSAR neutral organics model are 4540 and 789 mg/l. No measured data for either of these materials are available.

The toxicity of the related materials n-butyronitrile and isobutyronitrile to *Selenastrum capricornutum* was tested in 72-hour limit studies, which conformed to OECD test guideline 201 and were given reliability ratings of 1 (valid without restriction) (Eastman Kodak, 1999, 2000). Nominal concentrations of 200 mg/l were tested in both studies. The analytically measured concentrations of n-butyronitrile and isobutyronitrile were 133.4 and 87.8 mg/l (mean), respectively. There was no effect of treatment on growth rate or biomass; therefore, the EC50 values were higher than the concentrations that were tested. Both of these concentrations are within an order of magnitude of the EC50 concentrations calculated by ECOSAR for these materials (365 and 430 mg/l, respectively). Based on this relationship, it is expected that the experimental EC50 concentration for TDPN toxicity to algae would be no lower than 450 mg/l (10 times less than the ECOSAR-estimated value of 4540 mg/l).

4.3.4 Summary/Test Plan for Ecotoxicity

LC50 and EC50 toxicity values have been estimated by EPIWIN ECOSAR for fish, Daphnia and green algae. The values for all three species are > 4540 mg/l. Since results of experimental studies with the related materials propionitrile, butyronitrile and isobutyronitrile show EC/LC50 values that are within an order of magnitude of ECOSAR-predicted values, it is expected that the EC/LC50 value for the most sensitive species (i.e. algae) would be > 450 mg/l. This is four times greater than 100 mg/l, a concentration considered essentially non-toxic. Considering the use of this material as closed system, industrial intermediate, the low amounts present in waste water discharged from the plant, the limited production facilities in the US (see Appendix I), and the low level of concern based on the ECOSAR prediction, aquatic toxicity testing on this material is unnecessary. Therefore, no aquatic toxicity testing is planned.

4.4 Human Health Data

4.4.1 Acute Mammalian Toxicity

This endpoint is filled by sufficient oral, inhalation and dermal toxicity studies in rodents. The LD50 value for the oral study in mice conducted with thiodipropionitrile of > 90% purity is 3.75 g/kg (Tusing, 1953a). Inhalation exposure to a saturated vapor of thiodipropionitrile (containing approximately> 15.5 ppm) for 6 hours did not cause death or signs of toxicity in rats, mice or guinea pigs (Tusing, 1953b). The dermal LD50 value in guinea pigs was > 8 ml/kg (8.876 g/kg) (Tusing, 1953a).

Signs of toxicity in mice orally exposed to lethal concentrations included squinting, lacrimation, rapid and labored respiration, ataxia and depression, vasodilation around the mouth, mild clonic convulsions and coma preceding death. Postmortem examinations of mice that died revealed hemorrhagic or hyperemic lungs, distended stomachs, irritated intestines (with vasodilation in some cases), mottled livers and granular kidneys. In addition, blood clots were observed in the region of the transverse sinuses of 2 mice treated with 4.4 g/kg. No other brain damage was observed grossly. Animals that survived until necropsy had normal gross pathology.

4.4.2 Repeated Dose Mammalian Toxicity

Two repeated dose toxicity experiments have been performed with thiodipropionitrile.

Results of a 10-day repeated dose dermal study in rabbits show that application of 1.0 g/kg/day did not cause toxicity in 5/6 animals (Tusing, 1953a). After 6 treatments, one animal developed an apparent weakness or incoordination of the hind extremities. This behavior persisted until study termination. Placement and righting reflexes in this animal were normal. This animal also developed diarrhea, weight loss, and an "unthrifty" appearance. There were no significant necropsy findings in any of the animals (including the animal with diarrhea).

Rats have been given 100, 1,000 and 10,000 ppm thiodipropionitrile in the diet for 32 continuous days (Tusing, 1953b). Based on the average amount of food consumed and average body weights, the amount of test material consumed on a mg/kg/day basis was 10.7, 104.8 and 1010.8 for the 100, 1,000 and 10,000 ppm groups, respectively. In this study, the authors concluded that there was no evidence of toxicity at any dose level. However, one animal exposed to 100 and another to10,000 ppm died during the study. In addition, gross pathological changes in the liver and kidneys were observed in animals treated with 1,000 and 10,000 ppm. Since this study was not conducted according to current standards, it was given a reliability rating of 4 (not assignable).

Although these studies are not up to current standards, no further repeat dose testing is required, given use of the material as a closed system intermediate, the low concentration of TDPN present in the waste stream leaving the two plants, the non-volatile nature of TDPN, the protective equipment necessary due to the presence of acrylonitrile in the plant, and the low levels of TDPN found in downstream products and wastewater (see Appendix I). Existing repeated dose toxicity data are considered adequate considering the extremely low probability of exposure.

4.4.3 Genetic Toxicity

4.4.3.1 Mutagenicity

An OECD Test Guideline 471 test with 50 to 5000 micrograms/plate TDPN of 97.6% purity has been performed on 4 strains of *S. typhimurium* (TA98, TA100, TA1535 and TA1537) and *E. coli* strain WP2uvrA- (Thompson and Bowles, 2004). TDPN did not cause an increase in mutations, either in the presence or absence of metabolic activation. No additional testing is necessary.

4.4.3.2 Chromosomal aberration

An OECD Test Guideline 473 chromosomal aberration test was performed in rat lymphocytes with concentrations of TDPN ranging from 0 to 1420 micrograms/ml (10 mM) (Charles et al., 2004). The material was dissolved in dimethylsulfoxide (DMSO) prior to use. Experiments were conducted in the presence or absence of metabolic activation (with a 4 hour treatment period followed by a 20 hour recovery period) and in the absence of metabolic activation (with a 24 hour treatment period). In each experiment, there was no effect of test material on the frequency of cells with aberrations at any dose level.

4.4.4 Reproductive and Developmental Toxicity

Reproductive or developmental toxicity tests with thiodipropionitrile have not been performed. Thiodipropionitrile is used exclusively as a closed-system (Type A) industrial intermediate, chemically converted to other products. The potential for significant human exposure is strictly limited. Therefore it is believed that this material qualifies for exemption from reproductive toxicity testing under the established guidelines of the U.S. EPA HPV chemical program. Detailed documentation of the information required to substantiate manufacture and use as a closed-system industrial intermediate with limited exposure is provided in Appendix I of this test plan.

According to the U.S. EPA HPV Chemical program for Type A intermediates, developmental toxicity testing is required. However, due to the precautions involved in use and manufacture of the material (see Appendix I), the possibility for exposure is extremely low. Therefore, developmental toxicity testing is not necessary.

4.4.5 Additional Data

4.4.5.1 Skin and Eye Irritation

The results of a repeated dose dermal toxicity study in rabbits with material of fairly high purity (> 90%) indicate that 1.0 ml/kg thiodipropionitrile is not irritating to skin (Tusing, 1953b). In an acute study, application of 4.0 ml/kg (but not 8.0 ml/kg) to rabbits caused behavior indicative of burning or pain (Tusing, 1953a). Application of undiluted material to rabbit eyes caused pain, vascularization of the sclera and nictitating membrane and some edema of the upper eyelid that resolved within an hour.

4.4.5.2 Sensitization

The ability of thiodipropionitrile to produce sensitization was tested in modified repeated dose dermal toxicity study in rabbits (Tusing, 1953b). Test material (1.0 ml/kg) was applied dermally 5 days/week for a total of 10 applications, and a challenge dose of 1.0 m/kg was applied after a 10 day rest period. None of the rabbits tested exhibited any evidence of sensitization over the next 5 days.

4.4.6 Summary/Test Plan for Mammalian Toxicity

Adequate acute toxicity studies have been conducted for thidiopropionitrile. Results of these studies show that exposure to fairly large amounts of thiodipropionitrile is required to produce acute toxicity. The material may cause irritation to the skin and eyes immediately after exposure, which quickly resolves. Results of recently conducted, OECD Test Guideline mutagenesis and chromosome aberration studies indicate that TDPN is not mutagenic or clastogenic.

Results of repeated dose oral and dermal toxicity studies show that fairly high doses of thiodipropionitrile are required to produce toxicity. However, microscopic analyses and laboratory tests that are currently required of repeated dose toxicity studies were not performed.

Although these studies are not up to current standards, no further repeat dose testing is proposed, since the substance is a Type A industrial intermediate. No reproductive or developmental toxicity data are available, but no testing is planned for these endpoints, since the substance is a Type A industrial intermediate with extremely low probability of exposure (see Appendix I).

5. Summary

Physical properties

Adequate data exist to characterize melting point, boiling point, water solubility and partition coefficient. A value for the partition coefficient (log Kow) has been estimated using the EPIWIN KOWWIN program. No physical property testing is proposed.

Environmental fate properties

EPIWIN modeling provides adequate data for hydroxyl radical induced atmospheric photodegradation and environmental transport, as well as bioconcentration factor and Henry's Law Constant. Thiodipropionitrile is known to have limited stability in water and hydrolyses to the corresponding thiodipropionic acid (CAS No. 111-17-1) or its salt, depending on pH and temperature. Measured data indicate that the material does not biodegrade and hydrolysis occurs slowly at ambient temperatures.

Aquatic toxicity

Testing in fish, Daphnia or algae has not been performed with TDPN, but has been conducted with the related materials propionitrile, butyronitrile and/or isobutyronitrile. LC/EC50 values estimated by ECOSAR for the aforementioned alkyl nitriles in these species are within an order of magnitude of measured values. Therefore, it is expected that the EC/LC50 value for TDPN for the most sensitive species (i.e. algae) would be > 450 mg/l, which is 10-fold lower than the estimated value. Acute aquatic testing is not proposed for TDPN in fish, daphnia and algae, since this value is four times greater than that regarded as nontoxic to aquatic species (100 mg/l) and substantially greater than concentrations of TDPN in wastewater (See Appendix I for further documentation).

Mammalian toxicity

Adequate acute mammalian toxicity, mutagenesis and chromosome aberration data are available. No reproductive or developmental toxicity studies are available, but no testing is proposed, because thiodipropionitrile is manufactured and used exclusively as a site limited, closed system (Type A) industrial intermediate, extra precautions are taken to limit worker exposure, volatility is low, and concentrations of TDPN in downstream products and wastewater are negligible(See Appendix I for further documentation). Repeat dose studies are available and summarized. Although these studies are not up to current standards, no further repeat dose testing is required, since the substance is a Type A industrial intermediate with very low probability of exposure.

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APPENDIX I

Documentation of manufacture and use of thiodipropionitrile as an industrial intermediate

According to the EPA Guidance for Testing Closed System Intermediates for the HPV Challenge Program, "any chemical which is intended to undergo a further deliberate reaction to produce another industrial substance is considered an intermediate."

It is believed that thiodipropionitrile is a closed system intermediate that fits the description of a Type A closed system industrial intermediate. This description is as follows:

(a) isolated intermediates which are stored in controlled on-site facilities

The EPA guidance also states that documentation is to be provided to support the claim for reduced testing. Such documentation includes information on number of sites, basis for closed process, and information on release, transportation or presence in distributed product. This information for thiodipropionitrile is provided below:

Thiodipropionitrile is manufactured at two plant sites in the United States. These sites are owned and operated by Cytec Industries Inc. and The Dow Chemical Company (one site per company). At each site, manufacture is carried out in a closed system by the reaction of acrylonitrile with sodium sulfhydrate (SSH) in an aqueous medium. During the reaction, no additional water is added to the reactor. The total number of workers involved in the manufacture and use processes at the two plant sites is approximately 40 for Dow and 8 for Cytec Industries Inc. The reactants are each added to the reactor from closed feed tanks through closed lines. A slight molar excess of SSH is employed to assure complete chemical conversion of acrylonitrile. The reaction temperature is maintained between 28-30ºC, since thiodipropionitrile undergoes significant hydrolysis to thiodipropionic acid and its sodium salt at higher temperatures. Since the reaction vessel is maintained at temperatures slightly above ambient, one would not expect a release to generate a condensation aerosol.

The product liquid thiodipropionitrile layer is purified by water washing and separation within the closed reactor, and transported through closed lines to a storage tank. From the storage tank, thiodipropionitrile is transferred on site through closed lines to another reactor for conversion to a different chemical used to manufacture thio chemicals. In addition to the liquid product layer, the reaction process has three other process layers, which are the aqueous alkaline layer containing excess SSH, and two water washes. The water washes are recycled to the process and any waste aqueous layers are sent to plant waste process water treatment facilities for biodegradation. These streams contain minimal concentrations of thiodipropionitrile. Analyses of the water streams from 5+ batches of TDPN have detected 0.10-2.52% TDPN present in the water streams. The major organic component of these streams is byproduct waste, thiodipropionic acid, sodium salt, which is formed by hydrolysis of the product.

Analysis of downstream products made from TDPN revealed less than 0.1% TDPN (the level of detection) in four different lots. In another analysis of three downstream products with greater analytical sensitivity, there was no TDPN at a detection level of 5 ppm. Products derived from TDPN are not marketed to consumers as produced but are part of formulations. Thus, the concentrations of TDPN that would be expected in the final products are much, much lower.

The waste water streams from products derived from TDPN have been found to contain not detectable (< 2 ppm) to 80 ppm TDPN. The TDPN waste streams are subsequently diluted at least a 100-fold, resulting in a maximum estimated concentration of 25 ppm in the waste water treatment plant. The amount of TDPN in the water exiting the waste water treatment plant is below the detection limit of 2 ppm. The solid waste residue from the production operations and treatment plant does not contain detectable amounts of TDPN (< 2 ppm).

Although no industrial hygiene monitoring data are available for thiodipropionitrile at either manufacturing facility, the closed system manufacturing and conversion processes, coupled with the limited volatility (saturated vapor concentration at 25^{o}C is <0.1 ppm) and high boiling point (163-4ºC at 1 hPa) of thiodipropionitrile both suggest that any worker exposure to this substance would be infrequent and at a very low level. Extra precautions must be taken (closed system, engineering controls, personal protective clothing as appropriate, etc.) to comply with special, strict Occupational Safety and Health Administration (OSHA) regulations (29 CFR 1910.1045) designed to prevent exposure to acrylonitrile, the raw material used to manufacture TDPN. These regulations have been in place since 1980. The current OSHA TLV for acrylonitrile is 2 ppm. As required by the OSHA regulations, whenever the concentration of acrylonitrile is unknown, a supplied air and auxiliary self-contained breathing apparatus with full facepiece in positive pressure mode is required to minimize exposure to acrylonitrile vapor. In addition, impermeable protective clothing (includes impervious gloves and an apron to prevent skin contact, chemical splash-proof goggles or a face shield, and a NIOSH approved respirator when there is potential for inhalation exposure) is used to protect any area of the body which may come in contact with liquid acrylonitrile (Cytec Industries Inc., 1997). During maintenance in these plants, workers are required to wear a complete suit to minimize exposure to acrylonitrile. In addition, all employees exposed to acrylonitrile at concentrations at or above the action level of 1 ppm are required to be part of a medical surveillance program. The protective equipment worn to reduce/eliminate exposure to acrylonitrile, a more volatile material, should minimize worker exposure to thiodipropionitrile.

In conclusion, at both Cytec Industries Inc. and the Dow Chemical Company, the sole use of TDPN is as a closed system industrial intermediate, which is completely converted to other thio chemicals at the same plant site. There are no sales of TDPN, the intermediate does not leave the manufacturing site at either company, and TDPN is not present appreciably in any downstream product. Protective clothing worn to prevent exposure to acrylonitrile will minimize worker exposure to TDPN. The waste water streams from TDPN or products derived from TDPN have been found to contain < 100 ppm TDPN. The amount of TDPN in the water exiting the waste water treatment plant is below the detection limit of 2 ppm.